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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/709,045	11/10/2000	M. Rigdon Lentz	LEN 102	3239

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EXAMINER	
SPECTOR, LORRAINE	
ART UNIT	**PAPER NUMBER**
1647	

DATE MAILED: 07/12/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/709,045	LENTZ, M. RIGDON	
	Examiner	Art Unit	
	Lorraine Spector, Ph.D.	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 April 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,5,8-11 and 17-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,5,8-11 and 17-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. *4/13/04* .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Part III: Detailed Office Action

Claims 1-3, 5, 8-11, and 17-22 are pending and under consideration.

In view of the revised priority claim, the instant application merits priority to the filing date of Application 09/083307, filed 5/22/98. The Selinsky reference previously cited under 35 U.S.C. §103 (Immunology 1998) was published in May of that year, and received by the USPTO on 5/28/1998. Accordingly, that reference is no longer available under 35 U.S.C. §103.

New rejections apply.

Formal Matters:

Claim 18 is objected to as being grammatically incorrect; the phrase "antibodies is" should be amended to read "antibodies are".

The specification is objected to because the relationship between this application and application 09/699003, filed 10/26/2000, is not stated. Priority claims made under 35 U.S.C. §120 must include the relationship, i.e. continuation, divisional, or continuation in part. See MPEP 201.11. Similarly, the priority statement states that application 09/316,226 "claims priority" from application 09/083,307.

Applicant is also required to update the status of all applications to which priority is claimed. Application 09/083307 issued as a U.S. Patent on 9/16/2003.

Correction is required.

Double Patenting:

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 2, and 8-11 are rejected under the judicially created doctrine of double patenting over claims 1-8 of U. S. Patent No. 6,231,536 since the claims, if allowed, would improperly extend the "right to exclude" already granted in the patent.

The subject matter claimed in the instant application is fully disclosed in the patent and is covered by the patent since the patent and the application are claiming common subject matter, as follows: The claims differ only in the permutations in which the various claim limitations occur, but are coextensive with each other.

Furthermore, there is no apparent reason why applicant was prevented from presenting claims corresponding to those of the instant application during prosecution of the application which matured into a patent. See *In re Schneller*, 397 F.2d 350, 158 USPQ 210 (CCPA 1968). See also MPEP § 804.

Claims 5, and 17-22 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-8 of U.S. Patent No. 6,231,536. Although the conflicting claims are not identical, they are not patentably distinct from each other because with respect to claim 5, it is old and routine in the art to combine therapeutic modalities in the treatment of cancer; thus the method of claim 5 is obvious over the patented claims. With respect to claims 17-22, the claims are broader than the patented claims. However, as the patented species anticipates the currently claimed 'genus', a finding of obviousness type double patenting is proper.

Claims 1-3, 5, and 8-11 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-9, and 12-14 of U.S. Patent No. 6,620,382. Although the conflicting claims are not identical, they are not patentably distinct

from each other because the patented claims read on a method of removing soluble TNF receptor from blood or plasma using an absorbent column, see especially claims 7 and 13. Note that the '382 specification states that :

"Additional, and/or selective, removal of these molecules can be obtained using antibody, or antibody fragments (single chain, recombinant, or humanized), immunoreactive against the receptor molecules."

Accordingly, read in light of the specification, the claims include single chain, recombinant and humanized antibodies.

With respect to claims 17-22, the claims are broader than the patented claims. However, as the patented species anticipates the currently claimed 'genus', a finding of obviousness type double patenting is proper.

Applicants argument pertaining to the '536 patent in the response filed 4/16/2004 has been fully considered but is not deemed persuasive, as claim 5 of the patent states that the molecules are removed by binding of the molecules to a filter, claim 6 requires that the molecules removed are sTNF-R-1 or –2, and claim 7 states that such are removed "by binding to the cytokine or to an antibody or antibody fragment immunoreactive with the cytokine receptor molecules." Thus, the currently claimed method is anticipated by the patented claims. Molecular weight exclusion would not result in binding to an antibody, contrary to applicants argument.

With further respect to applicants arguments, if applicants wish to file a terminal disclaimer to overcome the double patenting rejections, such must be done *before*, and not after any interference proceedings, as no interference proceeding will be declared so long as the claims are under rejection for double patenting.

Claims 1-3, 5, 8-11 and 17-22 remain provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-5, 8-10, 12 and 16-20 of copending Application No. 09/699003. Although the conflicting claims are not

identical, they are not patentably distinct from each other because for reasons of record in the Office Action mailed 2/25/2004.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Objections and Rejections under 35 U.S.C. §112:

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 17-21 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The independent claim in question, claim 17, recites "contacting the plasma with antibodies specifically binding to a targeted immune system inhibitor". The specification does not use the term "targeted immune system inhibitor", nor can said term be said to flow from the specification as originally filed. The specification at page 1 discloses the invention as "generally in the field of enhancing an immune response, and particularly relates to the removal of TNF inhibitors in a patient....". The specification at page 3 discloses the invention as utilizing antibodies immunoreactive with TNFR-1 or –2, IL-2R, IL-1R, IL-6R or sIFN-gammaR. Additional species in the claims as originally filed are antibodies that bind to soluble receptors for GM-CSF, EPO, TPO, G-CSF, M-CSF and SCF, although there appears to be no antecedent basis for those species in the specification as originally filed. At page 5, beginning at line 26 of the specification, it is stated that "Selective removal or neutralization of the soluble cytokine receptors (which function as inhibitors of the cytokine." However, this is not disclosure of a genus of "immune system inhibitors". At page 9, the specification states "Based on the

presumed mechanism that the process is removing immune inhibitors produced by the tumors, especially inhibitors of cytokines and other immune mediators...". This disclosure of a possible mechanism is *not* tantamount to a disclosure of a method of removing any possible immune system inhibitor, as in claim 17. The broadest reasonable reading of the specification is that the disclosure is limited to methods of removing immune inhibitors produced by tumors. Accordingly, claim 17 constitutes new matter, as it is not limited to such.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-3, 5, 8-11, and 17-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is indefinite because the antecedent basis for the second recitation of "soluble cytokine receptor molecules" at line 5 of the claim is not clear, or alternatively, because the phrase is redundant. Further, the recitation of "antibodies or antibody fragments binding to soluble cytokine receptor molecules" is indefinite because it is not clear whether the soluble cytokine receptor molecules are being co-administered, i.e. whether "binding" is a verb, or alternatively whether "binding" is an adjective, and applicants intend that the antibodies or antibody fragments are able to bind to cytokine receptors. Claim 17 is similarly indefinite at part ©. There is insufficient antecedent basis in claim 1 for "the cytokine receptor" at lines 5-6 of the claim; the only aforementioned receptors are *soluble* cytokine receptors, and due to the amendment to the claim, there are two different mentions of such. There is no antecedent basis for "the cytokine" in line 9 of claim 1.

Claim 5 is indefinite because it is not clear how the step of claim 5 relates to the method of claim 1; there is no interrelationship between the steps. Similarly, claim 8 is indefinite because it is not clear from what the cytokine receptor molecules are removed, *which* cytokine receptor molecules of claim 1 are being removed (unclear antecedent basis), nor when this step occurs (lack of interrelationship between steps of the method).

Claim 17 recites "contacting the plasma with antibodies specifically binding to a targeted immune system inhibitor" The specification does not use nor define the term "immune system inhibitor", hence the metes and bounds of the claim cannot be determined.

Claim 19 is indefinite as an antibody cannot be a fragment. The antibody is the whole, and the fragment is a part of the whole.

The remaining claims are rejected for depending from an indefinite claim.

Rejections Over Prior Art:

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 8, 9, and 11 are rejected under 35 U.S.C. 102(e) as being anticipated by Bohm et al., U.S. Patent Number 5,817,528.

Bohm et al. teach a sterile and pyrogen-free column containing coupled protein for binding and removal of substances from blood. Preferred proteins are antibodies (column 4 lines 10-19). The use of anti-interferon antibodies is also disclosed as being useful for treatment of autoimmune diseases, allergy and transplant rejection (column 2 lines 23-31). As treatment of such condition would reduce the amount of diseased tissue in the patient, the claims are anticipated by Bohm et al. It is noted that anti-interferon antibodies are within the metes and bounds of "soluble cytokine receptor molecules", as they are soluble, and bind to the cytokine interferon.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 10 and 17-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bohm in view of Schneider, U.S. Patent Number 4,512, 763 and further in view of U.S. Patent Number 5,565,332 (Hoogenboom et al.) . The teachings of Bohm are reviewed above. Bohm does not teach separation of plasma prior to removal of substances from blood, nor recombinant, fragment or humanized antibodies.

It is noted that Howell, U.S. Patent Number 6,379,708 defines interferons Beta and alpha-2b as immune system inhibitors, see column 2. Accordingly, the anti-IFN antibodies taught by Bohm et al. would meet the limitations of claim 17.

Schneider teaches the separation of plasma from other blood components prior to the removal of immune complexes or other constituents, see sentence bridging columns 2-3. The person of ordinary skill in the art would immediately recognize that interferon would be found in the plasma fraction, as it is a soluble molecule.

Hoogenboom et al. disclose humanized antibodies and methods of making such. At col. 1 lines 16-30 they disclose the advantages of such as being overcoming the problem of elicitation of anti-globulin response when a non-human antibody is administered to a human. See also col. 3 lines 8-15 in this regard. At column 2 lines 57+, they disclose that antibody fragments can

perform the function of whole antibodies, and set forth single chain antibodies as being examples of antibody fragments.

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to modify the teachings of Bohm to (a) separate the plasma from the cellular components prior to subjecting the plasma to the column containing the antibodies, and (b) to substitute fragment or humanized antibodies for the antibodies taught by Bohm . The person of ordinary skill in the art would have been motivated to make the former modification in order to avoid subjecting the cellular components of blood to the inevitable shearing and other forces inherent to the immunoadsorbant column, and would have been motivated to make the latter modification in view of the possibility of some of the antibody detaching from the column and entering the bloodstream; the person of ordinary skill in the art would immediately recognize the advantages to avoiding any possible anti-Ig response in the patient, as taught by Hoogenboom. Further, one would be motivated to use antibody fragments as taught by Hoogenboom, in view of their inherent advantages; ease of production especially, in the case of single-chain antibodies, which are antibody fragments. Accordingly, the invention, taken as a whole, is *prima facie* obvious over the prior art.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Bensinger teaches a method of removing blood from a patient, separating the removed blood into plasma and cellular components, passing the plasma component through an immunoadsorbent material to produce a treated plasma component, and returning the treated plasma component and the cellular component to the patient (see abstract). In the background of the invention it is disclosed that the method is specifically for removal of immune complexes from patients with tumors, and Stapylococcus Protein A is a preferred immunoadsorbant.

Advisory Information:

No claim is allowed.

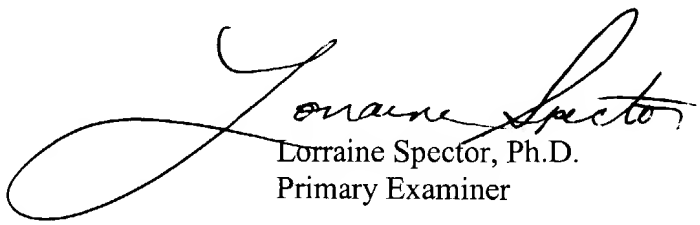
Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Lorraine M. Spector. Dr. Spector can normally be reached Monday through Friday, 9:00 A.M. to 3:00 P.M. ***Effective 1/21/2004, Dr. Spector's telephone number is 571-272-0893.***

If attempts to reach the Examiner by telephone are unsuccessful, please contact the Examiner's supervisor, Ms. Brenda Brumback, at telephone number 571-272-0961.

Certain papers related to this application may be submitted to Group 1800 by facsimile transmission The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). NOTE: If Applicant does submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Official papers filed by fax should be directed to (703) 872-9306 (before final rejection) or (703)872-9307 (after final). Faxed draft or informal communications with the examiner should be directed to ***571-273-0893.***

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Lorraine Spector, Ph.D.
Primary Examiner